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| (21) International Application Number: PCT/US99/13755 (22) International Filing Date: 18 June 1999 (18.06.99) (30) Priority Data: 60/089,852 19 June 1998 (19.06.98) US | | (81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i> | |
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| (54) Title: PROCESSES TO GENERATE SUBMICRON PARTICLES OF WATER-INSOLUBLE COMPOUNDS | | | |
| (57) Abstract | | | |
| Submicron particles of water-insoluble compounds, particularly drugs, are prepared by simultaneously stabilizing microparticulate suspensions of same with surface modifier molecules by rapid expansion into an aqueous medium from a compressed solution of the compound and surface modifiers in a liquefied gas and optionally homogenizing the aqueous suspension thus formed with a high pressure homogenizer. | | | |

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 99/13755

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K9/16 A61K9/51 A61K9/14

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| E | WO 99 52504 A (HOFFMANN LA ROCHE) 21 October 1999 (1999-10-21) the whole document --- | 1-16 |
| A | WO 97 14407 A (RES TRIANGLE PHARMACEUTICALS ;UNIV TEXAS (US); HENRIKSEN INGE B (U) 24 April 1997 (1997-04-24) cited in the application the whole document --- | 1-16 |
| A | WO 95 21688 A (WEIDNER ECKHARD ;KNEZ ZELJKO (SI); NOVAK ZORAN (SI)) 17 August 1995 (1995-08-17) --- | |
| A | US 3 998 753 A (ANTOSHKIW THOMAS WILLIAM ET AL) 21 December 1976 (1976-12-21) --- | -/- |

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Patent family members are listed in annex.

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Int'l. Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|----------|--|-----------------------|
| A | G. DONSI ET AL.: "POSSIBILITY OF APPLICATION TO PHARMACEUTICAL FIELD" PHARM. ACTA HELV, 1991 - 1991, pages 170-173, XP002900588 ----- | |

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/13755

| Patent document cited in search report | | Publication date | Patent family member(s) | | Publication date |
|--|---|------------------|-------------------------|--|------------------|
| WO 9952504 | A | 21-10-1999 | NONE | | |
| WO 9714407 | A | 24-04-1997 | AU 709262 B | | 26-08-1999 |
| | | | AU 7461796 A | | 07-05-1997 |
| | | | EP 0855906 A | | 05-08-1998 |
| WO 9521688 | A | 17-08-1995 | SI 9400079 A | | 31-10-1995 |
| | | | AT 159184 T | | 15-11-1997 |
| | | | CA 2182786 A | | 17-08-1995 |
| | | | DE 59500808 D | | 20-11-1997 |
| | | | DK 744992 T | | 02-06-1998 |
| | | | EP 0744992 A | | 04-12-1996 |
| | | | ES 2109095 T | | 01-01-1998 |
| | | | GR 3025495 T | | 27-02-1998 |
| | | | JP 9508851 T | | 09-09-1997 |
| US 3998753 | A | 21-12-1976 | AT 351912 B | | 27-08-1979 |
| | | | AT 625675 A | | 15-01-1979 |
| | | | BE 832331 A | | 12-02-1976 |
| | | | DE 2534091 A | | 26-02-1976 |
| | | | FR 2281961 A | | 12-03-1976 |
| | | | GB 1502895 A | | 08-03-1978 |
| | | | IT 1050722 B | | 20-03-1981 |
| | | | JP 51041732 A | | 08-04-1976 |
| | | | NL 7509586 A | | 17-02-1976 |